REMARKS

Applicants respectfully request reconsideration of the application, as amended, in view of the following remarks.

The claims are neither anticipated nor obvious over WO 00/66122 and Peyman (US 6,489,335). WO 00/66122 and Peyman fail to disclose or suggest methods for treating dry eye, ocular discomfort and ocular surface damage as claimed in which an ophthalmic composition comprising from about **0.01% to about 0.06%** of FK506 is administered to a patient who, prior to treatment, has a superficial punctate keratitis (SPK) score of at least two. See Claims 15, 16 and 18.

The present specification discloses that patients having the claimed score respond well to the treatment of the present invention. That is, those patients have a high sensitivity to a certain concentration of FK 506. For example, the specification discloses at page 4, lines 9-14:

> Moreover, the present inventor has discovered that patients having Schirmer scores less that about 7 to less than about 5 millimeters per five minutes and/or **superficial punctuate keratitis scores of greater than or equal to 2** or greater than or equal to 3 **respond particularly well to treatment**.

In addition, the specification discloses at page 15, line 31 to page 16, line 3:

> Preferred patients are those having a Schirmer score of less than 7 millimeters per five minutes and/or a superficial punctuate keratitis (SPK) score of at least 2. The most responsive patients, however, are those having a Schirmer score of less than 5 millimeters per five minutes and/or an SPK score of at least 3.

Further, the Examples show the following as disclosed at page 17, lines 15-22:

> The results of the lissamine green staining at day 42 showed an improvement over baseline in macrolide-treated patients having a Schirmer score of less than 5 millimeters/five minutes and an SPK score of at least 3. While placebo-treated patients showed decreases of 0.6 ± 3.15 units from baseline, patients treated with **0.01% and 0.06** macrolide compound, showed decreases of 1.8 ± 1.47 units and 3.9 ± 2.03 units, respectively.

In contrast, WO 00/66122 and Peyman do not disclose that patients having the claimed SPK score are highly sensitive to a specific concentration of FK 506.

Therefore, the rejection of Claims 1-14, 17 and 18 under 35 U.S.C. § 102(b) as anticipated by WO 00/66122, and the rejection of Claims 15, 16 and 19 under 35 U.S.C. § 103(a) as being unpatentable over WO 00/66122 and Peyman (US 6,489,335) are believed to be unsustainable as the present invention is neither anticipated nor obvious and withdrawal of these rejections is respectfully requested.

Applicants traverse the double patenting rejections. None of the claims of U.S. 6,872,383 or Serial No. 09/926,411 disclose or suggest the required amount of **0.01% to about 0.06%** of FK506 or the required SPK score prior to treatment as claimed in the present application.

In the present invention, a specific concentration of FK 506 is effective for patients suffering from moderate-to-severe dry eye. In the present invention, **the patients suffering from moderate-to-severe dry eye are limited to those having a specific SPK** (superficial punctate keratitis: fine abrasion of cornea developed due to dry eye) **score of at least two.** Examples describe that 0.01-0.06 % of the present compound has an improving effect in the patients having moderate-to-severe SPK scores associated with dry eye.

On the other hand, U.S. 6,872,383 describes an improving effect on Tear Break-up Time (BUT), which evaluates quality and quantity of tears. However, the reference does not describe whether it is effective for patients suffering from moderate-to-severe dry eye, who have fine abrasions due to the dry eye, such as superficial punctate keratitis (SPK). This, the double-patenting rejections should be withdrawn.

Applicants respectfully request that the Examiner acknowledge that the references cited in the **Information Disclosure Statement, filed** in the above-identified application on **August 23, 2004,** have been considered.

This application presents allowable subject matter, and the Examiner is kindly requested to pass it to issue. Should the Examiner have any questions regarding the claims or otherwise wish to discuss this case, he is kindly invited to contact Applicants' below-signed representative, who would be happy to provide any assistance deemed necessary in speeding this application to allowance.

Respectfully submitted,

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LIST OF REFERENCES CITED BY APPLICANT		APPLICANT Ryuji UENO	
		FILING DATE January 16, 2004	GROUP 1614

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB CLASS	FILING DATE IF APPROPRIATE
	AA	5,514,686	05/07/1996	M. MOCHIZUKI, et al.			
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						
	AL						
	AM						
	AN						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION YES	TRANSLATION NO
	AO	WO 03/043650	05/30/2003	WIPO		
	AP	WO 00/66122	11/09/2000	WIPO		
	AQ	WO 02/085359	10/31/2002	WIPO		
	AR	0 484 936	05/13/1992	EUROPE		
	AS					
	AT					
	AU					
	AV					

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, etc.)

	AW	FUJISAWA, XP-002230797, 2 pages, "FUJISAWA PROTOPIC (TACROLIMUS) FOR DERMATOLOGIC USE ONLY NOT FOR OPHTHALMIC USE", December 2000
	AX	
	AY	
	AZ	

☐ Additional References sheet(s) attached

Examiner	Date Considered

*Examiner: Initial if reference is considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.